

## A broad-spectrum synthesis of Tetravinylethylenes

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# A Broad-Spectrum Synthesis of Tetravinylethylenes

Kelsey L. Horvath,<sup>[a]</sup> Christopher G. Newton,<sup>[a]</sup> Kimberley A. Roper,<sup>[a]</sup> Jas S. Ward<sup>[a]</sup> and Michael S. Sherburn<sup>\*[a]</sup>

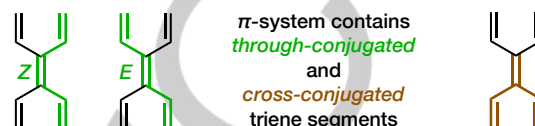
**Abstract:** The first general synthesis of compounds of the tetravinylethylene (TVE) family is reported. Ramirez-type dibromolefination of readily accessible penta-1,4-dien-3-ones generates 3,3-dibromo[3]dendralenes, which undergo twofold Negishi, Suzuki-Miyaura or Mizoroki-Heck reactions with a wide variety of olefinic coupling partners. This route delivers a broad range of unsymmetrically-substituted tetravinylethylenes with up to three different alkenyl substituents attached to the central C=C bond. The extensive scope of the approach is demonstrated by the preparation of the first higher order oligo-alkenic through-conjugated/cross-conjugated hybrid compounds. An unsymmetrically-substituted TVE is shown to undergo a domino electrocyclic-cycloaddition with high site-selectivity and diastereoselectivity, thereby demonstrating the substantial synthetic potential of substituted TVEs for controlled, rapid structural complexity generation.

Tetravinylethylene (TVE) is one of the smallest structures exhibiting both through-conjugation and cross-conjugation (Scheme 1). Specifically, the structure comprises intersecting pairs of (*E*)-1,3,5-hexatrienes, (*Z*)-1,3,5-hexatrienes and 2-methylene-1,4-pentadienes ([3]dendralenes). Nothing is known about the impact of substitution upon the behavior of TVEs and how this might be exploited. Furthermore, related structures containing more than five C=C units have not been reported in the literature. The first synthesis of TVE, a landmark contribution from the classical era of unsaturated hydrocarbon chemistry, was reported by Skattebøl and co-workers in the 1960s.<sup>1-3</sup> We recently disclosed the first preparatively useful approach to TVE, a one-step multi-gram scale synthesis, and demonstrated that the hydrocarbon is bench-stable when stored as a neat liquid.<sup>4,5</sup> The one-step synthesis of TVE (Scheme 1, **1a**) utilized a Pd(0)-catalyzed fourfold Stille cross-coupling sequence between tetrachloro-ethylene **2** and vinyltributylstannane **3a**. In addition to the parent TVE, five symmetrically-substituted TVEs **1b** were similarly prepared using substituted alkenyltributylstannanes **3b** in the exhaustive Stille cross-coupling process.<sup>4,5</sup>

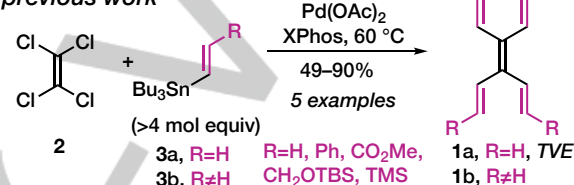
As a starting point for future synthetic applications, the parent TVE has been shown to rapidly generate multi-cyclic systems.<sup>4,5</sup> Additionally, the hybrid through/cross-conjugated structure of the TVE unit represents the smallest organic four-directional branch point in a possible conducting molecular wire.<sup>6</sup> To realize the potential of the TVE family in target synthesis and materials applications, synthetic access to unsymmetrically-substituted systems must be granted. Until now, no unsymmetrically-substituted TVEs have been reported. Our previous synthetic approach (Scheme 1), in common with all other substituted TVE

syntheses reported in the literature,<sup>7</sup> is only suited to the attachment of four identical substituted alkenyl-groups to the central C=C core.

## introduction to TVE

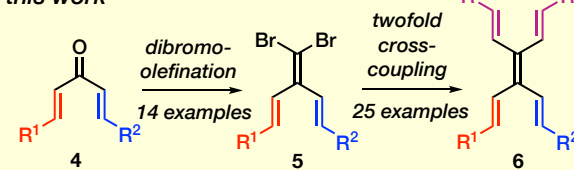


## previous work<sup>4,5</sup>



• fourfold Stille approach to TVE and symmetrically-substituted TVEs

## this work



• first synthesis of unsymmetrically-substituted TVEs  
• di-, tetra-, hexasubstituted TVEs with up to 3 different substituents  
• no organotin: Negishi, Suzuki-Miyaura, Mizoroki-Heck reactions

**Scheme 1.** The existing synthetic route to TVEs with its limitations, and the new, broad scope synthesis.

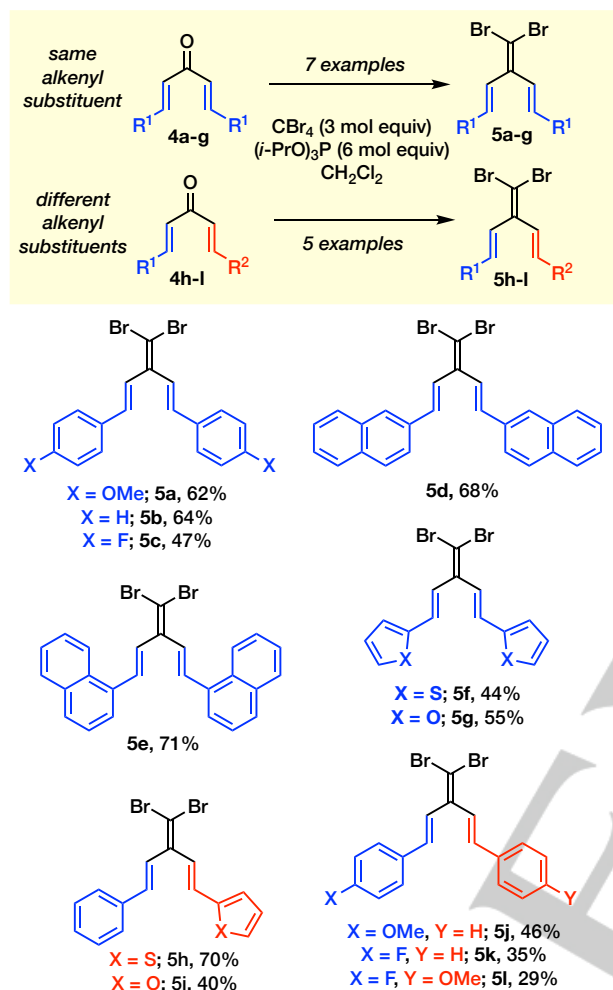
Herein we report a broad-reaching solution, delivering the first 29 unsymmetrically substituted TVEs carrying up to three different substituents (Scheme 1, bottom). We also report the first compounds exhibiting extended  $\pi$ -systems based upon TVE subunits. Moreover, we establish the synthetic potential of these unsymmetrically-substituted TVEs, by way of a one-pot, site-selective and diastereoselective domino pericyclic sequence that generates three C–C bonds and six contiguous stereocenters. The new synthetic approach (Scheme 1, bottom) involves the conversion of penta-1,4-dien-3-ones **4** (readily accessed through twofold aldol-type condensations) into 3,3-dibromo[3]dendralenes **5**, which in turn undergo a range of twofold cross-couplings to furnish diversely-substituted tetravinylethylenes **6**.

Twelve substituted penta-1,4-dien-3-ones **4** were prepared, by way of sequential Claisen-Schmidt condensations<sup>8</sup> (see SI for details). There are only three examples of Ramirez dibromolefinations of penta-1,4-dien-3-ones **4** in the literature<sup>9-11</sup> and, in our hands, low yields were obtained under standard Ramirez reaction conditions.<sup>12</sup> Gratifyingly, in the majority of cases, the modified protocol introduced by Lautens and co-workers<sup>13</sup>

[a] Kelsey L. Horvath, Dr Christopher G. Newton, Dr Kimberley A. Roper, Dr Jas S. Ward, Prof Michael S. Sherburn\*  
Research School of Chemistry  
Australian National University  
Canberra, ACT 2601 (Australia)  
E-mail: [michael.sherburn@anu.edu.au](mailto:michael.sherburn@anu.edu.au)

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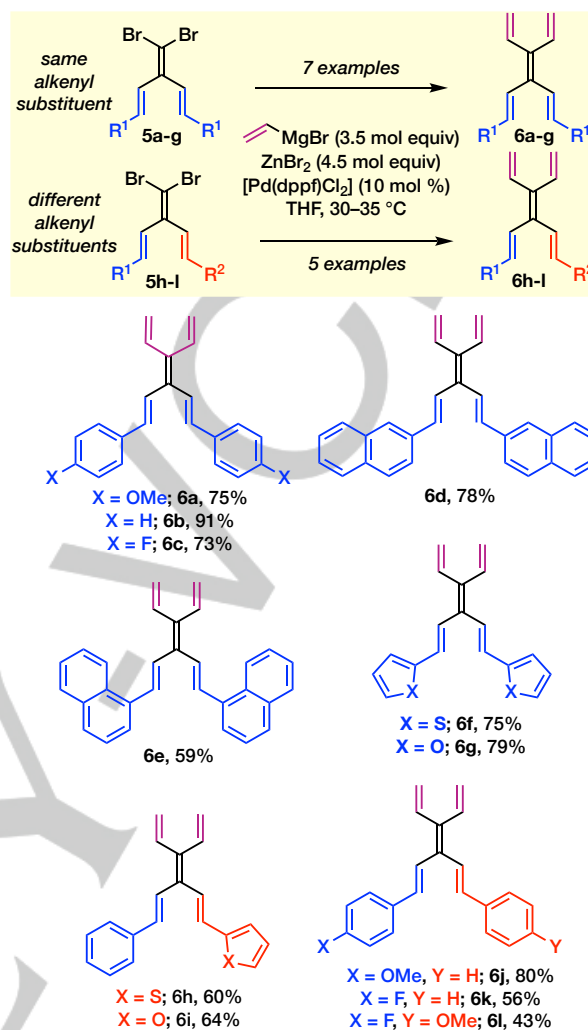
furnished workable yields, and twelve substituted 3,3-dibromo[3]dendralenes<sup>14</sup> **5** were prepared in this manner (Table 1).



**Table 1.** Lautens-modified Ramirez dibromo-olefination of penta-1,4-dien-3-ones **4** permits the first general synthesis of 3,3-dibromo[3]dendralenes **5**.

Unlike some other dendralenic structures, which exhibit a propensity to dimerize and polymerize,<sup>15</sup> 3,3-dibromo[3]dendralenes **5** are generally white or yellow crystalline solids that can be stored neat without appreciable decomposition, and are easily handled using standard laboratory techniques.

While there are many examples of cross-coupling reactions of 1,1-dibromoalkenes in the literature,<sup>16</sup> there is only one example of a cross-coupling of a 3,3-dibromo[3]dendralene, involving the Sonogashira  $sp^2$ – $sp$  coupling of a cyclic system with trimethylsilylacetylene.<sup>10</sup> In light of the lack of precedent, both for  $sp^2$ – $sp^2$  cross-couplings and also for reactions of acyclic systems, we were delighted to find that twofold Negishi reactions of 3,3-dibromo[3]dendralenes **5** with vinylzinc bromide proceed well using  $[\text{Pd}(\text{dppf})\text{Cl}_2]$  as pre-catalyst to form the first unsymmetrical TVEs **6** (Table 2).



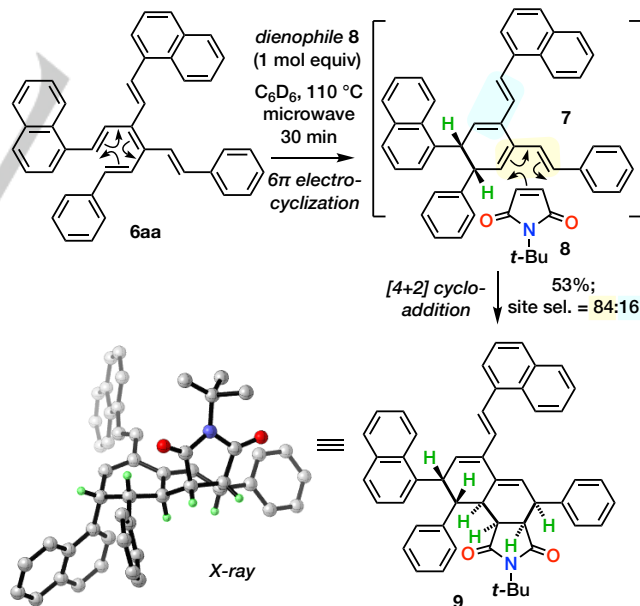
**Table 2.** Twofold Negishi cross-coupling of 3,3-dibromo[3]dendralenes **5** with vinylzinc bromide furnishes the first unsymmetrical tetravinylethylenes **6**.

3,3-Dibromo[3]dendralenes comprising the same (**5a-g**) or different (**5h-l**) alkenyl substituents performed equally well, to generate the first examples of TVEs possessing two or three different alkenyl groups about the central C=C bond. TVEs bearing carbocyclic aromatic substituents with different electronic characteristics (**6j-l**) and the first TVEs carrying heterocyclic aromatic substituents (**6f-i**) are included in this selection.

Twofold cross-couplings of 3,3-dibromo[3]dendralenes **5** are by no means limited to the introduction of a pair of unsubstituted vinyl groups: in fact, alkenyl groups bearing substituents at any position are tolerated. The syntheses of eighteen of these more highly substituted TVEs are summarized in Table 3. Double Negishi couplings of 3,3-dibromo[3]dendralene **5a** with 2-propenyl-, (*E*)-styrenyl- and (2-methylprop-1-en-1-yl)zinc bromides furnished six novel tetra- and hexa-substituted TVEs **6n-s**. Cross-couplings other than Negishi reactions are also successful, as demonstrated by the products of double Suzuki-Miyaura<sup>17</sup> and Mizoroki-Heck<sup>18</sup> processes, **6t-v** (3 examples)

Following the trend previously seen,<sup>4,5</sup> the 25 new TVEs depicted in Tables 2 and 3 are bench-stable substances. No special equipment or methods are required when manipulating these compounds: they survive storage neat at ambient temperature for several weeks. The lack of susceptibility of this new family of  $\pi$ -bond rich systems towards uncatalyzed Diels-Alder dimerization and autoxidation (typical of related cross-conjugated<sup>15</sup> and through-conjugated<sup>19</sup> polyenic systems) bodes well for future applications.

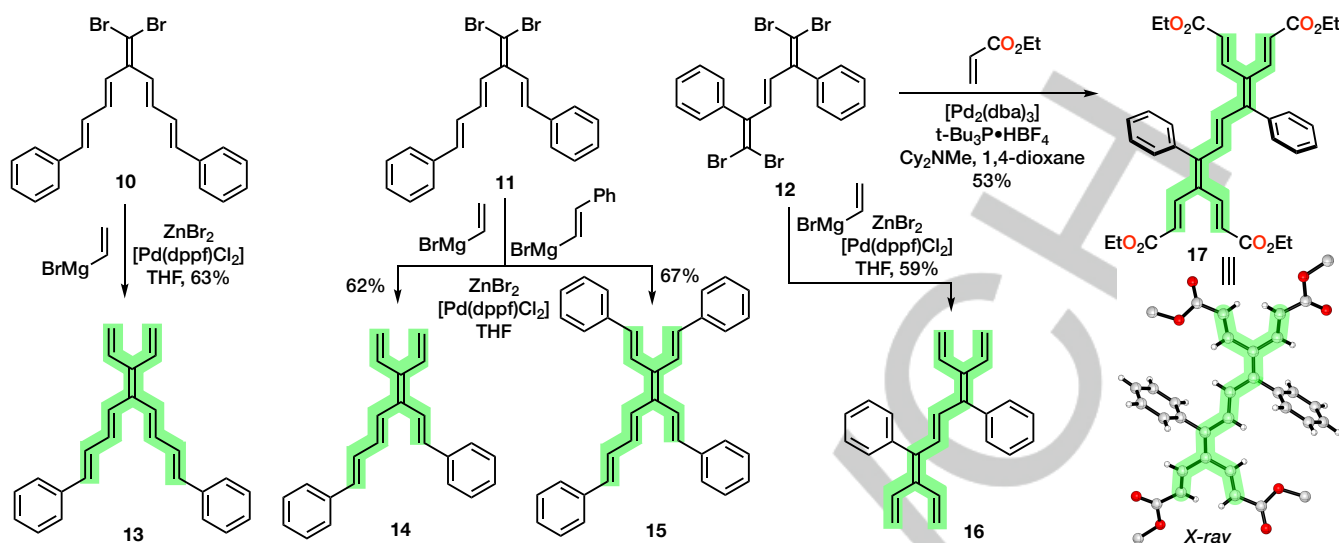
Access to unsymmetrically-substituted TVEs promotes new opportunities in rapid structure complexity generation, and an interesting question of diene site selection in [4+2]cycloadditions of polyenes (Scheme 2). Heating diphenyl-di-(1-naphthyl)-TVE **6aa** in benzene brings about a disrotatory electrocyclization to generate cyclic [4]dendralene<sup>14</sup> **7**, with a *cis*-disposition between the two cyclohexadiene substituents. When performed in the presence of dienophile *N*-*tert*-butylmaleimide **8**, a subsequent *endo*-mode cycloaddition occurs, with approach to the less sterically encumbered  $\pi$ -diastereoface of [4]dendralene **7**. The two non-equivalent semi-cyclic dienes of [4]dendralene **7** (highlighted in different colors in Scheme 2) are expected to be more reactive than the cyclohexadiene site,<sup>5</sup> and the phenyl-substituted diene is preferred over the 1-naphthyl-substituted site. Overall, this operationally trivial domino sequence generates densely-functionalized decalin **9**, with three new C–C bonds, six contiguous stereocenters, and a cyclic [3]dendralene subunit that invites additional synthetic manipulation.<sup>20</sup>



**Scheme 2.** Stereoselective domino [6 $\pi$ ]electrocyclization/[4+2]cycloaddition of TVE **6ad** proceeds with diene site selectivity to generate multicyclic product **9**. H atoms not attached to stereocenters are omitted from the X-ray crystal structure<sup>22,23</sup> for clarity.

**Table 3.** Twofold Negishi, Suzuki-Miyaura or Mizoroki-Heck reactions grant access to unsymmetrical, multi-substituted tetravinylethylenes. <sup>a</sup>X-ray crystal structures of these four TVEs<sup>22</sup> are in the SI.





**Scheme 3.** First preparation of higher order acyclic C=C-based  $\pi$ -frameworks related to TVE. The new  $\pi$ -systems are highlighted in green. Ethyl groups are truncated in the X-ray crystal structure<sup>22,23</sup> for clarity.

The robust nature of the new pentaene-based TVE compounds, combined with their ease of synthesis, prompted the question of whether larger structures with unprecedented acyclic  $\pi$ -frameworks were within reach. The successful extension of these methods to the syntheses of hexaenes **14** and **15**, and heptaenes **13**, **16** and **17** are depicted in Scheme 3. Dibromotetraene **10**, dibromo-pentaene **11** and tetrabromo-triene **12**, prepared through Lautens-modified Ramirez dibromo-olefination reactions of commercially available ketonic precursors (see SI), underwent twofold or fourfold Negishi or Mizoroki-Heck couplings to furnish the bench-stable polyenic products. The UV absorption spectrum of heptaene **17** exhibits features attributable to the longest through-conjugated subunit (see SI). The solid state molecular structure of tetra-ester **17**, obtained from single crystal X-ray analysis, is consistent with this observation, revealing an essentially in-plane 2,4,6,8,10-dodecapentaenoate unit (Scheme 3). Acyclic, hybrid cross-conjugated/through-conjugated C=C structures are very poorly represented in the literature.<sup>21</sup> The structures depicted in Scheme 3 represent the first examples of substances of this type.

In summary, we have described the first general synthetic approach to TVEs and related through/cross-conjugated acyclic C=C-based systems. This work reports 34 new TVEs and related structures, including the first examples exhibiting unsymmetrical substitution patterns, extended through-conjugation and/or cross-conjugation. The synthetic approach is robust, involving twofold Negishi, Suzuki-Miyaura or Mizoroki-Heck couplings of acyclic 3,3-dibromo[3]dendralenes. The new structures are bench stable compounds that undergo operationally simple, selective, complexity-generating domino sequences. The acyclic C=C-bond-rich structures described herein are representatives of a sizeable region of structural space that was previously inaccessible but is now available for exploration and investigation. Applications in target synthesis and in conducting materials will follow.

## Acknowledgements

This work was supported by the Australian Research Council.

**Keywords:** hydrocarbons • polyenes • cross-coupling • electrocyclic reactions • cycloaddition

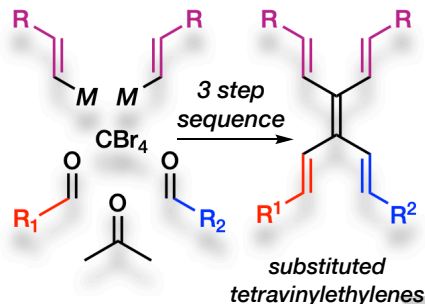
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## Entry for the Table of Contents

## COMMUNICATION

**Master key for TVE.** The first general synthesis of tetravinylethylenes (TVEs) involves the preparation and cross-coupling of dibromo-[3]dendralenes. Their value in controlled, rapid structural complexity generation is demonstrated. The first higher order acyclic oligo-alkenic through-conjugated/cross-conjugated hybrid compounds are also reported.



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